REMARKS

I. Claim Status

Claims 1-40 are pending. Without prejudice or disclaimer, in accordance with 37 C.F.R. §§ 1.1821-1.825, Applicants have amended (1) the specification to incorporate by reference the Sequence Listing submitted herewith; (2) ¶ [0028] of the specification to provide the SEQ ID NOs for Figures 4A, 4B, and 4C; (3) ¶ [0030] of the specification to provide the SEQ ID NOs for Figures 6A and 6B; and (4) Table 6 on page 28 of the specification to provide a SEQ ID NO for the RO-TAMRA nucleotide sequence (i.e., SEQ ID NO:8) and the SEQ ID NOs for the other nucleotide sequences in Table 6 have been renumbered to put them in the proper numerical order because of the addition of the SEQ ID NO for the RO-TAMRA nucleotide (i.e., nucleotides CO (SEQ ID NO:9), B7-67mer (SEQ ID NO:10), T3 (SEQ ID NO: 11), and SM (SEQ ID NO:12)).

In addition, Applicants submit herewith substitute sheets of the amended computer readable form (CRF) of the Sequence Listing adding the RO-TAMRA nucleotide used in Example 6 and identified in Table 6 as SEQ ID NO:8 and renumbering the nucleotides following it to put them in proper numerical order.

In accordance with 37 C.F.R. § 1.825(a), Applicants respectfully submit that the amendments to the specification, including Table 6, and the substitute CRF of the Sequence Listing include no new matter as the RO-TAMRA nucleotide used in Example 6 was originally identified in Table 6, including its nucleotide sequence, of the application as-filed, but its SEQ ID NO was inadvertently omitted from Table 6 and the Sequence Listing as-filed.

No claims are amended herein.

Thus, no new matter is presented herein.

II. Objections to Drawings

The Examiner objects to the drawings because:

a. The lettering is not of proper size, uniform density, and well-defined in Figures 1-4, 6, 8, 9, and 11;

b. The lines are not clean, well-defined, and of uniform thickness in Figures 1-4 and 6-9;

c. Each panel needs to be individually labeled, e.g., FIG. 2A, 2B, 2C, etc.; and

d. The Figures are not properly labeled (37 CFR 1.84(u)(1)); see FIG. 1, FIG. 3, FIG. 5, and FIGS. 7-11.

July 13, 2009, Office Action at 2. Applicants submit herewith replacement drawings satisfying the objections. Thus, Applicants respectfully submit that the objections to the drawings should be withdrawn.

III. Objection to the Specification

The Examiner objects to the specification because Table 6 "contains a representation of an oligonucleotide yet is not accompanied with the requisite SEQ ID NO." July 13, 2009, Office Action at 4. As noted above, Table 6 on page 28 of the specification has been amended to provide a SEQ ID NO for the RO-TAMRA nucleotide (i.e., SEQ ID NO:8) and the SEQ ID NOs for the other nucleotides in Table 6 have been renumbered to put them in the proper numerical order because of the addition of the SEQ ID NO for the RO-TAMRA nucleotide (i.e., nucleotides CO (SEQ ID NO:9), B7-67mer (SEQ ID NO:10), T3 (SEQ ID NO: 11), and SM (SEQ ID NO:12)). In addition, Applicants submit herewith substitute sheets of the amended Sequence Listing adding the RO-TAMRA nucleotide used in Example 6 and identified in Table 6 as SEQ ID NO:8 and renumbering the nucleotides following it to put them in proper numerical order. Thus, Applicants respectfully submit that the objection to the specification should be withdrawn.

IV. Rejection Under 35 U.S.C. § 112

The Examiner rejects claims 16-24 under 35 U.S.C. § 112 as allegedly failing to comply with the written description requirement for the reasons set forth on pages 4-7 of the July 13, 2009, Office Action. Specifically, the Examiner alleges that "the claims encompass an infinite number of complexes, including an infinite number of target nucleic acids, known and unknown," and states that the "specification provides a description of but two reported sequences and two target oligonucleotides." July 13, 2009, Office Action at 5. The Examiner concludes that the specification fails "to provide an adequate written description of the infinite number of intact complexes, with any and

all manner of fluorescent labels, much less an adequate written description of the target nucleic acids." *Id.*

Applicants respectfully traverse for the following reasons.

To begin with, Applicants respectfully note that they are not claiming "an infinite number of complexes, including an infinite number of target nucleic acids." Rather, while the number of target nucleic acids that can be identified and/or measured by the claimed nucleic acid complexes is only limited by the total number of targets that one wishes to identify and/or measure, the claimed nucleic acid complexes require specific structure, as described in the specification, which differentiates them from other nucleic acids, including target nucleic acids, that fall outside the scope of the claims. Indeed, contrary to the Examiner's position, interpreted from the vantage point of one skilled in the art, the specification describes the claimed invention in sufficient detail such that the skilled artisan would have been able to determine the structure of the claimed nucleic acid complexes and would have further concluded that the inventors had possession of the subject matter claimed at the time of filing of the application.

Claim 16, for example, recites:

> A nucleic acid complex comprising an **oligonucleotide hybridized** to a fluorophore-labeled reported sequence, wherein the oligonucleotide comprises **a hairpin-forming sequence capable of forming a stem-loop**, and wherein formation of the stem-loop modifies fluorescence signals of the reporter sequence when the reporter sequence is hybridized to the oligonucleotide.

(Emphasis added). The specification provides definitions for a number of terms used in the specification, including the following terms recited in claim 16: "oligonucleotide," "hybridize," "hairpin-forming sequence," and "stem-loop." *See* Specification as-filed at ¶¶ [0040], [0041], [0043], and [0050]. The definitions of each of these terms provide structure and physical properties of the claimed nucleic acid complexes sufficient to satisfy the written description requirement and distinguish the claimed complexes from those falling outside the scope of the claims. *See Regents of the Univ. of California v. Eli Lilly & Co.*, 119 F.3d 1559, 1566 (Fed. Cir. 1997) (citation omitted).

Furthermore, the specification provides a general methodology that can be used to easily make a claimed nucleic acid complex depending on the target nucleic acid.

For example, if you want to measure a particular target nucleic acid, the specification explains that three things may be done, all of which would have been well within the normal purview of one of skill in the art. First, a complementary sequence that will bind to the sequence of the target nucleic acid may be determined. *See, e.g.*, Specification as-filed at ¶¶ [0054] and [0060]. This would have been a routine and predictable step for one of skill in the art.

Second, once a complementary sequence is determined, a hairpin or stem-loop forming sequence, as defined in the specification, may be synthesized using standard nucleic acid synthesis techniques. *See, e.g., id.* Such hairpin or stem-loop forming sequences would also have been well known to one of skill in the art, and the specification provides at least one example using repeating "T" and "A"/"C" and "G" nucleosides on opposite sides of the hairpin, which also includes the capture oligonucleotide in its interior. *See, e.g., id.* at ¶ [0079].

Third, a reporter sequence that can be quenched may be determined. *See, e.g., id.* at ¶¶ [0054] and [0060]. The specification discloses one example of quenching—G-base quenching—which is defined as describing "the reduction in fluorescence emission of a fluorophore when in close proximity to guanosine bases in the sequence of a single or double-stranded nucleic acid." *See id.* at ¶ [0048]. One way to do this is to place three cytidine bases on the opposite side of the hairpin at the beginning of the hairpin. The cytidine bases and guanosine bases from opposite sides of the hairpin will bind. Again, one of skill in the art would have been able to easily determine the sequences to add to any capture sequence for a desired target.

Although recitation of sequences and examples are not necessary to satisfy the written description requirement in biotech applications (*see, e.g., Capon v. Eshhar*, 418 F.3d 1349 (Fed. Cir. 2005), and again in *Falko-Gunter Falkner v. Inglis*, 448 F.3d 1357 (Fed. Cir. 2006)), the specification discloses a sequence falling within the scope of the claimed invention and also discloses examples providing additional details of the claimed nucleic acid complexes which can be used to identify two target sequences, 24mer and B7-67mer. *See* Specification as-filed at ¶¶ [0073]-[0074].

While these examples provide further detail of the claimed invention, the written description is not limited to the specific nucleic acid complex disclosed in the

specification and examples. As the specification notes, "[a]lthough a single sequence is described, it is understood that thousands of these sequences can be made and tested simultaneously in a gene expression array." *See id.* at ¶ [0060]. One of skill in the art would have easily been able to use the same general methodology described above for any target molecule to produce a nucleic acid complex having an overall sequence that includes the quenching region, hairpin region, including capture sequence, and reporter complement, and which falls within the scope of the claims.

Indeed, once one of skill in the art determines the necessary sequences to be included in the claimed nucleic acid complex based upon the target sequence, commercial suppliers could have synthesized it using routine steps. For example, the specification used molecules provided by Integrated DNA Technologies, Inc. or Synthetic Genetics, Inc. (*see* Specification as-filed at ¶ [0068]), and other suppliers provide these services. The specification also discloses that computer programs, such as OligoAnalyzer 3.0, can be used to help ensure that the sequence to be made does not form self-dimers, unwanted hairpins, and cross-hybridization. *See* Specification as-filed at ¶ [0068].

Accordingly, despite the Examiner's assertions to the contrary, Applicants are not attempting to satisfy the written description requirement through obviousness. *See* July 13, 2009, Office Action at 7. Rather, as discussed above, the specification describes the claimed nucleic acid complexes using terms that provide specific structure and physical properties of the claimed nucleic acid complexes. The specification also provides a general methodology for making a claimed nucleic acid complex depending on the target nucleic acid one wishes to identify and/or measure. Finally, while not required, the specification provides non-limiting examples of the claimed nucleic acid complex, which provide further description of the claimed nucleic acid complex. Such description satisfies the written description requirement. Thus, Applicants respectfully submit that the rejection should be withdrawn.

Conclusion

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration of this application and the timely allowance of the pending claims.

If the Examiner believes a telephone conference could be useful in resolving any outstanding issues, the Examiner is respectfully invited to contact Applicants' undersigned counsel at (703) 776-9703.

Respectfully submitted,

J.A. LINDEMAN & CO. PLLC

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By: /Aaron M. Raphael, Reg. No. 47,885/
Aaron M. Raphael
Reg. No. 47,885